

Special Report Rapport spécial

The increasing risk of Lyme disease in Canada

Catherine Bouchard, Erin Leonard, Jules Konan Koffi, Yann Pelcat, Andrew Peregrine, Neil Chilton, Kateryn Rochon, Tim Lysyk, L. Robbin Lindsay, Nicholas Hume Ogden

Abstract – There is an increasing risk of Lyme disease in Canada due to range expansion of the tick vector, *Ixodes scapularis*. The objectives of this article are to i) raise public awareness with the help of veterinarians on the emerging and expanding risk of Lyme disease across Canada, ii) review the key clinical features of Lyme disease in dogs, and iii) provide recommendations for veterinarians on the management of Lyme disease in dogs.

Résumé – **Risque accru de maladie de Lyme au Canada.** Il existe un risque grandissant de maladie de Lyme au Canada en raison d'un élargissement de la portée de la tique vectrice, *Ixodes scapularis*. Les objectifs du présent article consistent à i) rehausser la sensibilisation du public avec l'aide des vétérinaires quant au risque émergent et grandissant de la maladie de Lyme au Canada, ii) examiner les principales caractéristiques cliniques de la maladie de Lyme chez les chiens et iii) présenter des recommandations aux vétérinaires pour la gestion de la maladie de Lyme chez les chiens.

(Traduit par Isabelle Vallières)

Can Vet J 2015;56:693–699

Lyme disease risk in Canada

Lyme disease (LD) is the most common tick-borne disease affecting human and dog health in North America and Europe (1). In most human cases, LD presents as a non-specific flu-like illness frequently with a characteristic skin lesion known as erythema migrans (2). If left untreated, the disease can progress to arthritic, cardiac, and neurological manifestations. In dogs, clinical disease is a less common outcome of infection than in humans and usually presents as one or more of: fever, anorexia, depression, lethargy, lameness, joint swelling, arthritis, and lymphadenopathy. Nephropathy can also occur in the

more advanced stages of the disease in dogs, although this is uncommon (3).

In Canada, the agent of LD is the spirochete *Borrelia burgdorferi sensu stricto*, which is transmitted by the bite of ticks in the genus *Ixodes*. *Ixodes scapularis*, the blacklegged tick, is the main vector in eastern and central North America and *Ixodes pacificus*, the western blacklegged tick, is the main vector west of the Rocky Mountains (2).

Recent studies suggest that LD is an emerging health risk in southeastern and south central Canada, mostly due to the increasing geographic range of *I. scapularis* (2,4–7). *Ixodes scapularis* feeds on a broad range of animal species including rodents, birds, medium- and large-sized mammals, and reptiles, and also humans (8). Immature (larval and nymphal) ticks become infected by feeding on wild animal reservoirs (particularly rodents such as the white-footed mouse, *Peromyscus leucopus*) and are capable of transmitting infection to humans or animals after they molt into nymphs or adults. The tick season in Canada is typically from the spring snow melt to late autumn, although different life-cycle stages are active at different times of the year, and onset and end of activity can vary among years and localities. In most cases, ticks must attach and feed for 24 to 48 h before *B. burgdorferi* transmission occurs (9,10).

In southern parts of the country, the incidence of reported LD cases in humans has been increasing, particularly in southern parts of Ontario, Quebec, Manitoba, and in locations in Nova Scotia. In 2004, there were an estimated 40 reported human cases of LD in Canada (11); this number rose to 682 reported human cases in 2013 (unpublished data). The incidence of clinical cases of LD in dogs in Canada is unknown. The seroprevalence of *B. burgdorferi* in dogs in Canadian provinces ranged from 0.00% to 2.15% (average 0.72%) according to a study in 2008 (12). It was assumed that 2/3 of positive

Public Health Risk Sciences Division, Laboratory for Foodborne Zoonoses (Bouchard, Pelcat, Ogden), and Zoonoses Division, Centre for Foodborne, Environmental and Zoonotic Infectious Diseases (Leonard, Koffi), Public Health Agency of Canada, Saint-Hyacinthe, Quebec and Ottawa, Ontario; Department of Pathobiology, University of Guelph, Guelph, Ontario (Peregrine); Department of Biology, University of Saskatchewan, Saskatoon, Saskatchewan (Chilton); Department of Entomology, University of Manitoba, Winnipeg, Manitoba (Rochon); Research Centre, Agriculture and Agri-Food Canada, Lethbridge, Alberta (Lysyk); Zoonotic Diseases and Special Pathogens, National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, Manitoba (Lindsay).

Address all correspondence to Dr. Catherine Bouchard; e-mail: cat.bouchard@gmail.com

Use of this article is limited to a single copy for personal study. Anyone interested in obtaining reprints should contact the CVMA office (hbroughton@cvma-acmv.org) for additional copies or permission to use this material elsewhere.

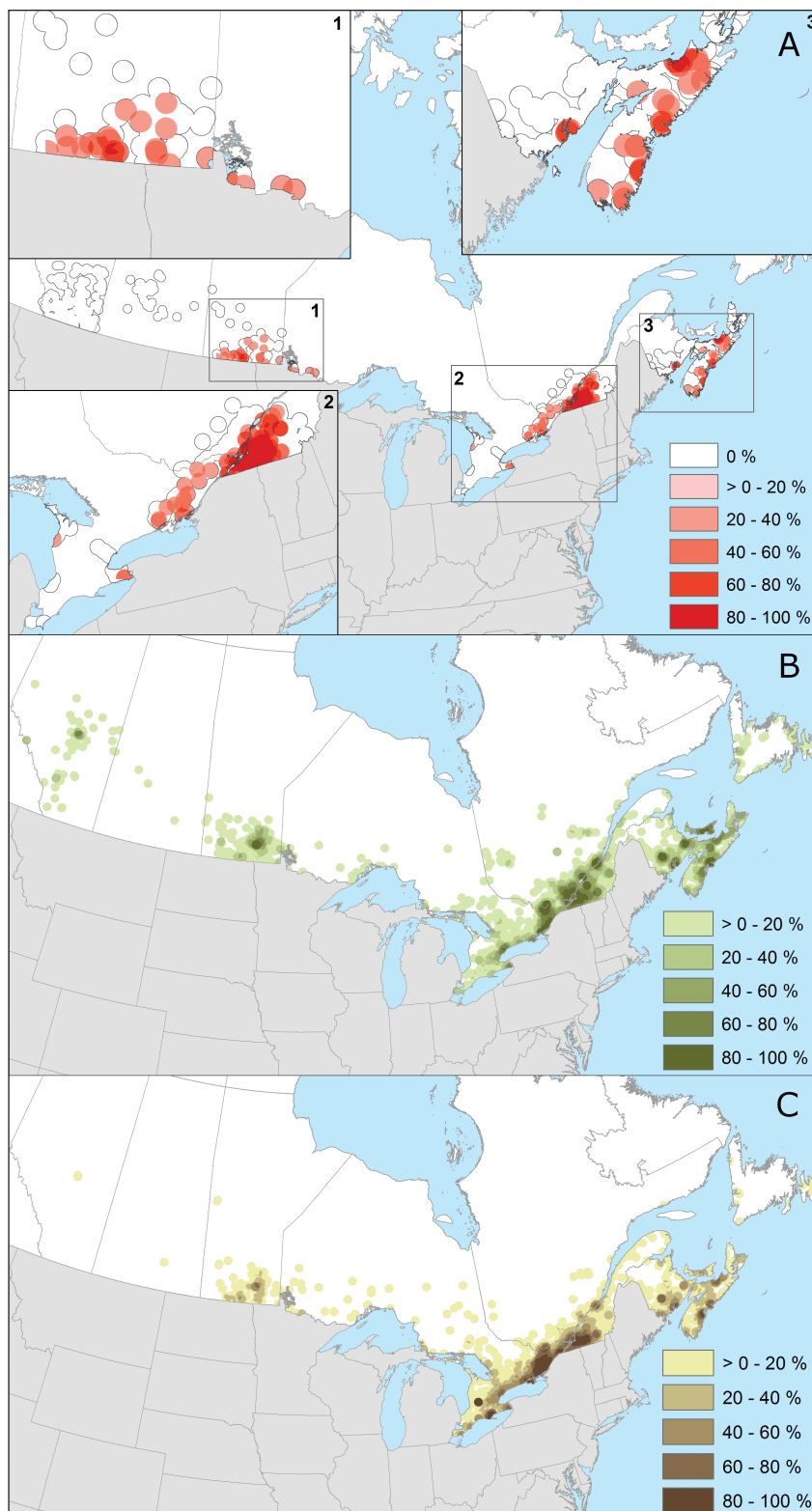


Figure 1. Surveillance for Lyme disease risk areas, and tick vectors in eastern and central Canada based on different surveillance systems: A – Active surveillance sampling sites visited from 2003 to 2012: site locations that were sampled are delimited by grey lines (buffer of 25 km created around each site) and the sites with at least 1 *I. scapularis* tick found are represented following a colored gradient and quintile classification (darker areas indicating higher numbers of sites with ticks). B – The geographic distribution of *I. scapularis* ticks submitted from dogs based on the probable locations of acquisition, 1991 to 2012: the locations with ticks submitted are represented following a green gradient and quintile classification (darker green areas indicate higher numbers of locations with ticks submitted). C – The geographic distribution of *I. scapularis* ticks submitted from humans based on the probable locations of acquisition, 1991 to 2012: the locations with ticks submitted are represented following a brown gradient and quintile classification (darker brown areas indicate higher numbers of locations with ticks submitted).

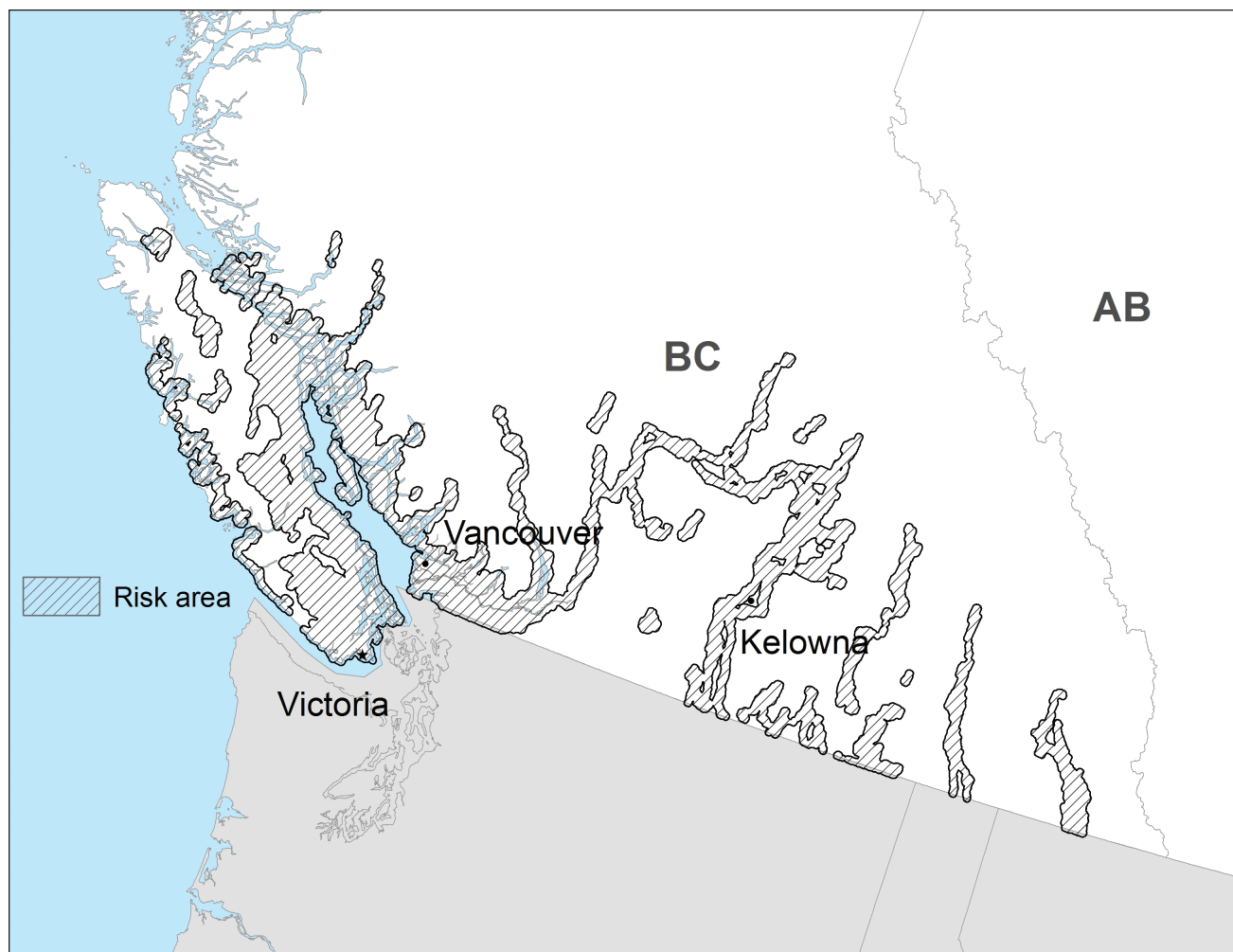


Figure 2. Lyme disease risk areas (hatched areas) where surveillance and research studies (risk mapping in BC: http://www.bccdc.ca/NR/rdonlyres/A07283DB-A709-4494-BFD5-E2AB7ED2724C/0/Lyme_Disease_Risk_Areas_Map_BC_June_2013.pdf) suggest ticks and *B. burgdorferi* have become established.

test results were associated with infections acquired in Canada, rather than being travel-acquired in LD risk areas outside the country. The low seroprevalence in Canada [in LD risk areas in the USA, seroprevalence is typically > 10% (13)] likely reflects the early stage of emergence of LD in Canada in 2008.

This article focuses on i) the environmental drivers of LD, ii) the geographic distribution and variation of LD risk areas in Canada, iii) the key clinical features and diagnostic options for detection of LD in dogs, and iv) recommendations for treatment and prevention of LD in dogs. Veterinarians across the country can play an important role in raising public awareness about ticks and the pathogens they transmit.

Environmental drivers

According to previous Canadian studies, the pattern of LD risk emergence and expansion is mostly shaped by the following environmental drivers: i) introduction of *I. scapularis* and *B. burgdorferi* by migratory birds (13–15); ii) climate conditions and climate warming that affect tick survival, activity, seasonality, and development (16,17); iii) habitat conditions that are suitable for host and tick populations (13,18,19); iv) density of *B. burgdorferi* reservoirs (e.g., the white-footed mouse,

Peromyscus leucopus) (7,20); v) density of deer populations, which drives the density of local vector populations (21,22); and vi) biodiversity of hosts and other community components affecting the *B. burgdorferi* transmission cycles (13,22,23).

In Canada, humans and animals are usually exposed to tick bites in deciduous woodlands, but also coniferous woodlands in the Maritimes (Lindsay, unpublished data) and elsewhere in the range of blacklegged ticks (24). Woodland habitats favor the survival of ticks by providing refuge from weather extremes, suitable hosts, and a microclimate suitable for survival and host-seeking (16). Host-seeking ticks climb woodland undergrowth vegetation and stretch out their forelegs to better “sense” potential hosts. However, pets and humans can also be exposed (albeit at lower frequencies) in urban and suburban settings (e.g., parks and gardens) due to ticks dispersed out of LD risk areas in woodlands by migratory birds (so-called “adventitious” ticks). These ticks pose a low-level but geographically widespread potential risk of exposure to LD-infected ticks.

Geographic distribution of LD risk areas

Canadian studies have used analysis of active field and passive tick surveillance data to identify expansion of the geographic

range of *I. scapularis* and emerging LD risk areas. Active field surveillance involves collecting ticks directly from the environment using drag sampling or capture of rodent hosts (11). Passive tick surveillance involves collecting ticks submitted from animals or humans through participating veterinary and medical clinics (5,11). In Canada, LD-endemic areas are locations where transmission of *B. burgdorferi* by resident populations of vector ticks has been confirmed by active surveillance (25). The number of documented endemic areas in which *I. scapularis* is the vector has increased from 1 location in Ontario in the 1970s, to 22 locations in 2014 in New Brunswick, Nova Scotia, Quebec, Ontario, and Manitoba, although the extent of likely risk areas (i.e., locations where a field study has found ticks) is much wider (Figure 1A) (11). Based on field surveillance data from 636 locations visited from 2003 to 2012, there are 3 regions with higher risk for LD across the country: i) southern Manitoba, ii) southern and eastern Ontario, and southern Quebec, and iii) parts of Nova Scotia and southern New Brunswick (Figure 1A). More details on the methodology for active sampling and the level of effort can be found in published studies (6,11,26).

Passive tick surveillance from 1991 to 2012 indicates the likely locations where ticks were acquired by pet dogs (Figure 1B) and humans (Figure 1C): a total of 16 288 *I. scapularis* ticks were collected from dogs and 9715 ticks were collected from humans. *Ixodes scapularis* ticks were found on dogs across Canada, from Newfoundland and Labrador to Alberta (Figure 1B). These maps show that the risk of dogs acquiring *I. scapularis* ticks is similar to that for humans (Figure 1C) and corresponds mostly to locations in which active surveillance has shown evidence of tick populations. However, because dogs are particularly effective at acquiring adventitious ticks (19), the geographic range of ticks collected in passive surveillance by veterinarians is wider than that of known reproducing tick populations (Figure 1B). Nevertheless, the regions with the highest risk of exposure to *I. scapularis* ticks for pets and humans are the southern parts of Manitoba, Quebec, and Ontario, and parts of the Maritimes.

In contrast, *I. pacificus* ticks are distributed widely throughout southern and central British Columbia (27). However, for several ecological reasons, the prevalence of *B. burgdorferi* in host-seeking *I. pacificus* ticks is relatively low (2). As a result, the probability of acquiring LD where *I. pacificus* ticks are the vector is much lower than the risk of acquiring LD where *I. scapularis* is the vector.

Geographic variation of LD risk

A range of landscape, climatic, and environmental factors have to converge for the co-existence of hosts, vectors, and transmission cycles of *B. burgdorferi* within a suitable habitat, and outside these broad limits significant LD risk cannot occur (28). However, these generalizations can break down on a fine geographic scale producing areas of uncharacteristically high or low environmental risk for LD. In Canada, the prevalence of *B. burgdorferi* in *I. scapularis* ticks varies regionally but is usually greater than 15% (sometimes reaching over 50%). Prevalence of infection may be less than 10% in locations where ticks and bacterium have only recently become established (29).

Table 1. Key clinical and diagnostic features to consider for possible LD in dogs

| Clinical features | Description |
|---|---|
| i) Clinical signs consistent with LD | <ul style="list-style-type: none"> Approximately 5% of dogs exposed to infected ticks develop clinical LD Most common clinical signs: fever, anorexia, depression, lethargy, sudden or recurrent lameness, joint swelling, myalgia, arthritis, and lymphadenopathy Clinical signs appear 2 to 5 mo after exposure Lyme nephritis, including immune-mediated glomerulonephritis and protein-losing nephropathy, can occur in later stages of the disease and more frequently in certain breeds of dogs (i.e., Labrador and golden retriever)^a |
| ii) Credible evidence of exposure to infected <i>Ixodes</i> tick(s) | <ul style="list-style-type: none"> Based on dog's history of activity in locations where exposure to <i>Ixodes</i> ticks is possible |
| iii) Positive laboratory tests | <ul style="list-style-type: none"> Most serological tests are not able to distinguish between active infection and exposure Antibodies can be detected in dogs between 3 and 5 wk after exposure to infected ticks and serological tests can remain positive for months and even over a year after infection (30,35)^b |
| iv) Elimination of other differential diagnoses | <ul style="list-style-type: none"> Many of the signs seen with LD could be due to other diseases [see algorithm in Littman et al (30)] |
| v) Response to treatment ^c | <ul style="list-style-type: none"> A decision flowchart for Lyme positive dogs and treatment recommendations can be found in Littman et al (30) and clinical veterinary medicine textbooks |

^a Less than 2% of seropositive dogs develop this disease with lameness reported in 9% to 28% of such cases (3); the conclusive involvement of *B. burgdorferi* has not been proven (37).

^b See further details in Diagnostic options section.

^c Some dogs with lameness due to other causes may respond to doxycycline treatment due to the drug's anti-inflammatory properties (30).

The prevalence of *B. burgdorferi* is typically less than 10% in *I. pacificus* ticks found in southern British Columbia (2).

There is an estimated 5-year delay between *I. scapularis* population establishment and *B. burgdorferi* establishment in southeastern Canada, but, due to particularities of the ecology of *I. scapularis*, this delay may be as short as 1 y in south central Canada (29). The percentage of infected ticks, therefore, is likely to increase with geographically variable rapidity in the years following establishment of *I. scapularis* tick populations in the south central and southeastern parts of Canada.

Key clinical features of LD in dogs

Clinical signs

Unlike humans, infection of dogs by *B. burgdorferi* infrequently results in clinical disease. Only about 5% of dogs develop clinical signs of LD when exposed to *B. burgdorferi* (30,31); the most common clinical signs in dogs are presented in Table 1. In other animals such as cats, horses, and cattle, serological responses to *B. burgdorferi* have been detected but the spectrum of clinical disease is less clearly defined for these species (32–34).

Diagnostic options

In dogs, confirmation of clinical LD through laboratory testing can be challenging (30,31,35); therefore, it is recommended that a LD diagnosis be based on 5 key criteria (Table 1).

The most common diagnostic test used to help confirm infection with *B. burgdorferi* is detection of specific antibodies to *B. burgdorferi* in serum. The serological assays are highly sensitive and specific, although detection of antibodies cannot be used to differentiate active infection from previous exposure to *B. burgdorferi* (30,31,35). Outcomes of serological testing need to be interpreted with care when the patient is from an area with low risk of exposure to *B. burgdorferi*-infected ticks, as false positives are likely to occur in this situation, leading to overdiagnosis (35,36).

One of the most commonly used serological tests is the C6 enzyme-linked immunosorbent assay (ELISA) which detects IgM and IgG antibodies circulating in the blood, and does not cross-react with antibodies generated in vaccinated animals; C6 antibody responses typically occur 3 to 5 wk following experimental infection in dogs (31,35). A quantitative C6 assay is also available which measures the amount of antibody to the *B. burgdorferi* C6 peptide circulating in the animal tested; declines in C6-specific antibodies following antibiotic treatment in dogs have been used as evidence of successful treatment in clinically ill dogs (35,37). Other less-used serological tests include whole cell ELISA, immunofluorescent antibody assays (IFA), and Western blotting. Whole-cell ELISA and IFA can give false-positive results, particularly when a dog has another spirochete infection, an inflammatory condition or has previously been vaccinated for LD (31,35,38). Western blot, which is commonly used in human medicine as a confirmatory test, has been used to differentiate natural infection and immunization response in dogs, but is more time consuming to complete and requires expertise to interpret, and therefore is not often used for standard diagnostic purposes in pets (31,35,38).

Other diagnostic testing that may or may not aid in clinical LD diagnosis include, but are not limited to, polymerase chain reaction (PCR), culture, complete blood (cell) count (CBC), biochemistry, and synovial fluid cytology. Multiple irregularities can be found on CBC and biochemical testing in dogs with Lyme nephropathy. However, other than proteinuria, the findings are highly variable and non-specific (35). Culture of *B. burgdorferi* from tissue or blood is the gold standard test for confirming *B. burgdorferi* infection; however, it has low sensitivity, requires long incubation periods (up to 6 to 8 wk), and is typically only used in research settings (30,31,35). The sensitivity and specificity of PCR testing in dogs are poorly defined and test performance characteristics in different diagnostic laboratories can vary. Also, PCR does not distinguish between viable and non-viable spirochetes (30,31,35). Contact your local animal health laboratory representative for more details on the test performance characteristics for the different LD diagnostic testing options mentioned here.

Treatment recommendations

According to the consensus statement of the American College of Veterinary Internal Medicine (ACVIM), treatment should

only be initiated in dogs displaying clinical signs consistent with LD, with evidence of exposure to LD risk areas and support from diagnostic laboratory tests (30) (Table 1). Treatment is also recommended in dogs with subclinical infections that are proteinuric. The standard treatment for LD in dogs is antibiotic therapy such as doxycycline for a minimum of 1 mo [10 mg/kg body weight (BW), PO, q24h] (31), although dogs with presumptive Lyme nephropathy may require longer courses of treatment (30). In young dogs, amoxicillin at 20 mg/kg BW, PO, q8h for 30 d may be used (31). Dogs will usually respond to treatment within a few days, provided infection is detected in the acute phase. However, in some cases, signs may return, and further treatment may be required (35,38).

Preventive measures

Since there is great regional variability in LD risk across the country and within each province, preventive measures should be encouraged where appropriate; recommendations for tick control should take into account the observed timing of infestations on pets in your practice area. Depending on the dog's activity and exposure to LD risk areas, pet owners should be advised of the following preventive measures:

- i) If possible, avoid high-risk areas during tick season (usually from spring snow melt to late autumn).
- ii) Check for ticks daily and promptly remove ticks after being in high-risk areas.
- iii) Peridomestic risk of exposure can be lowered by using a number of landscape management practices (e.g., removal of leaf litter, reduction of vegetative cover, and exclusion of wildlife using fences or other barriers) (39).
- iv) Routine use of acaricides (topical and oral anti-tick products, collars) when regularly exposed to high-risk areas. Some anti-ectoparasite products (e.g., those containing permethrin) are effective and safe for dogs but toxic for cats. The efficacy and safety of available anti-tick products vary and should be taken into consideration when choosing an appropriate product for pets. Refer to the specific safety and efficacy information available for each product and always follow the instructions for use provided on the product label.
- v) Routine vaccination when animals are regularly exposed to high-risk areas (available for dogs only); however, at present, the benefits of vaccinating dogs for Lyme disease, even in endemic areas, are debated (3). Some experts have concerns that since Lyme nephropathy has an immune-mediated pathogenesis, vaccination may increase the risk of generation of immune complexes and thus the risk of Lyme nephropathy in dogs predisposed to this condition (30,40,41). Multiple brands of vaccine to the outer surface proteins of *Borrelia burgdorferi* (OspA & OspC) are available for use in dogs; contact your pharmaceutical representatives for specific safety and efficacy information and recommendations.

In conclusion, veterinarians are a potentially key source of information for the public on the risk of Lyme disease and ticks. Dogs are often more exposed to ticks than are humans, and sero-positive dogs are typically detected sooner and in higher

numbers than human LD cases in emerging LD risk areas (42). Dogs may therefore be sentinels for early identification of emerging LD risk areas, allowing prompt implementation of activities to prevent human infections. Veterinarians can, therefore, play an important public health role in raising LD risk awareness.

Assessing risk in zones of emerging LD and endemic zones is challenging. The combination of active and passive surveillance systems has revealed increasing risk of LD in south eastern and south central Canada. However, the risk of infection can vary greatly across these regions. Veterinarians can use this information, as well as practice data and travel history, to adequately prevent/manage tick bites and LD cases in dogs. Information on regional, provincial, and federal public health organization websites (e.g., <http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/14vol40/dr-rm40-05/index-eng.php>) provides the most up-to-date information on LD risk areas in Canada.

Key points

- There is an increasing risk of Lyme disease in Canada following the expansion of the tick vector *I. scapularis* in southeastern and south central Canada.
- Lyme disease can affect the health of both humans and dogs — it is important that veterinarians be aware of the risk of Lyme disease for their patients as well as their owners.
- Dogs are more likely to be bitten by ticks but less likely to develop clinical signs of Lyme disease when compared to humans.
- Surveillance systems help to identify where the emerging and expanding Lyme disease risk areas are.
- The prevalence of *B. burgdorferi* infection in ticks varies across the country, being mostly greater than 15% in *I. scapularis* ticks and less than 10% in *I. pacificus* ticks.
- Prevention of Lyme disease is best accomplished through avoidance of ticks; frequent checks for ticks with prompt removal of attached individuals, routine use of tick-bite prevention products and potentially vaccination.
- Diagnosis of LD in dogs should be based upon clinical presentation, history of exposure to ticks and/or LD risk, and diagnostic testing results; treatment should be restricted to animals that present both clinical manifestations and diagnostic test results consistent with LD.

Acknowledgments

We thank our colleagues in provincial organizations who participated in the field and passive tick surveillance system (BC CDC, Alberta Health, Saskatchewan Health, Manitoba Health, Ontario Agency for Health Promotion and Protection, *Institut national de santé publique du Québec* and *Laboratoire de santé publique du Québec*, Université de Montréal, New Brunswick Agriculture, Aquaculture and Fisheries and New Brunswick Health, Nova Scotia Health and Wellness and Department of Natural Resources, Newfoundland & Labrador Department of Natural Resources), the Hastings & Prince Edward Counties, Chatham-Kent, Region of Peel, Niagara Region, County of

Lambton, Grey Bruce and Northwestern Health Units in Ontario who provided field surveillance data as well as individuals in Canadian universities, medical practitioners, veterinarians, and the public who submitted ticks.

cvj

References

1. Little SE, Heise SR, Blagburn BL, Callister SM, Mead PS. Lyme borreliosis in dogs and humans in the USA. *Trends Parasitol* 2010;26:213–218.
2. Ogden NH, Lindsay LR, Morshed M, Sockett PN, Artsob H. The emergence of Lyme disease in Canada. *Can Med Assoc J* 2009;180:1221–1224.
3. Littman MP. Lyme nephritis. *J Vet Emerg Crit Car* 2013;23:163–173.
4. Leighton PA, Koffi JK, Pelcat Y, Lindsay LR, Ogden NH. Predicting the speed of tick invasion: An empirical model of range expansion for the Lyme disease vector *Ixodes scapularis* in Canada. *J Appl Ecol* 2012;49:457–464.
5. Koffi JK, Leighton PA, Pelcat Y, et al. Passive surveillance for *I. scapularis* ticks: Enhanced analysis for early detection of emerging Lyme disease risk. *J Med Entomol* 2012;49:400–409.
6. Ogden NH, Bouchard C, Kurtenbach K, et al. Active and passive surveillance and phylogenetic analysis of *Borrelia burgdorferi* elucidate the process of Lyme disease risk emergence in Canada. *Environ Health Persp* 2010;118:909–914.
7. Bouchard C, Beauchamp G, Nguon S, et al. Associations between *Ixodes scapularis* ticks and small mammal hosts in a newly endemic zone in southeastern Canada: Implications for *Borrelia burgdorferi* transmission. *Ticks Tick-Borne Dis* 2011;2:183–190.
8. Tsao JI. Reviewing molecular adaptations of Lyme borreliosis spirochetes in the context of reproductive fitness in natural transmission cycles. *Vet Res* 2009;40(2):36. doi: 10.1051/vetres/2009019.
9. Schwan TG, Piesman J. Vector interactions and molecular adaptations of Lyme disease and relapsing fever spirochetes associated with transmission by ticks. *Emerg Infect Dis* 2002;8:115–121.
10. Cook MJ. Lyme borreliosis: A review of data on transmission time after tick attachment. *Int J Gen Med* 2015;8:1–8.
11. Ogden NH, Koffi JK, Pelcat Y, Lindsay LR. Environmental risk from Lyme disease in central and eastern Canada: A summary of recent surveillance information. *Public Health Agency of Canada. CCDR* 2014: 40–5.
12. Villeneuve A, Goring J, Marcotte L, Overvelde S. Seroprevalence of *Borrelia burgdorferi*, *Anaplasma phagocytophilum*, *Ehrlichia canis*, and *Dirofilaria immitis* among dogs in Canada. *Can Vet J* 2011;52: 527–530.
13. Bouchard C, Beauchamp G, Leighton PA, Lindsay R, Belanger D, Ogden NH. Does high biodiversity reduce the risk of Lyme disease invasion? *Parasit Vectors* 2013; Jul 1;6:195. doi: 10.1186/1756-3305-6-195.
14. Scott JD, Lee MK, Fernando K, Jorgensen DR, Durden LA, Morshed MG. Rapid introduction of Lyme disease spirochete, *Borrelia burgdorferi sensu stricto*, in *Ixodes scapularis* (Acari : Ixodidae) established at Turkey Point Provincial Park, Ontario, Canada. *J Vector Ecol* 2008; 33:64–69.
15. Ogden NH, Lindsay LR, Hanincova K, et al. Role of migratory birds in introduction and range expansion of *Ixodes scapularis* ticks and of *Borrelia burgdorferi* and *Anaplasma phagocytophilum* in Canada. *Appl Environ Microb* 2008;74:1780–1790.
16. Lindsay LR, Mathison SW, Barker IK, McEwen SA, Gillespie TJ, Surgeoner GA. Microclimate and habitat in relation to *Ixodes scapularis* (Acari : Ixodidae) populations on Long Point, Ontario, Canada. *J Med Entomol* 1999;36:255–262.
17. Ogden NH, Radojevic M, Wu XT, Duvvuri VR, Leighton PA, Wu JH. Estimated effects of projected climate change on the basic reproductive number of the Lyme disease vector *Ixodes scapularis*. *Environ Health Perspect* 2014;122:631–638.
18. Lindsay LR, Mathison SW, Barker IK, McEwen SA, Surgeoner GA. Abundance of *Ixodes scapularis* (Acari : Ixodidae) larvae and nymphs in relation to host density and habitat on Long Point, Ontario. *J Med Entomol* 1999;36:243–254.
19. Ogden NH, Barker IK, Beauchamp G, et al. Investigation of ground level and remote-sensed data for habitat classification and prediction of survival of *Ixodes scapularis* in habitats of southeastern Canada. *J Med Entomol* 2006;43:403–414.
20. Rogic A, Tessier N, Legendre P, Lapointe FJ, Millien V. Genetic structure of the white-footed mouse in the context of the emergence of Lyme disease in southern Quebec. *Ecol Evol* 2013;3:2075–2088.

21. Bouchard C, Leighton PA, Beauchamp G, et al. Harvested white-tailed deer as sentinel hosts for early establishing *Ixodes scapularis* populations and risk from vector-borne zoonoses in Southeastern Canada. *J Med Entomol* 2013;50:384–393.
22. Werden L, Barker IK, Bowman J, et al. Geography, deer, and host biodiversity shape the pattern of Lyme disease emergence in the thousand islands archipelago of Ontario, Canada. *Plos One* 2014;9:e85640. doi: 10.1371/journal.pone.0085640
23. Ogden NH, Tsao JI. Biodiversity and Lyme disease: Dilution or amplification? *Epidemics-Neth* 2009;1:196–206.
24. Lee X, Coyle DR, Johnson DK, et al. Prevalence of *Borrelia burgdorferi* and *Anaplasma phagocytophilum* in *Ixodes scapularis* (Acari: Ixodidae) nymphs collected in managed red pine forests in Wisconsin. *J Med Entomol* 2014;51:694–701.
25. Laboratory Centre for Disease Control. Consensus conference on Lyme disease, Health Canada, Guelph, Ontario, January 15–16, 1991.
26. Rochon K, Scoles GA, Lysyk TJ. Dispersion and sampling of adult *Dermacentor andersoni* in rangeland in Western North America. *J Med Entomol* 2012;49:253–261.
27. Mak S, Morshed M, Henry B. Ecological niche modeling of Lyme disease in British Columbia, Canada. *J Med Entomol* 2010;47:99–105.
28. Reisen WK. Landscape epidemiology of vector-borne diseases. *Annu Rev Entomol* 2010;55:461–483.
29. Ogden NH, Lindsay LR, Leighton PA. Predicting the rate of invasion of the agent of Lyme disease *Borrelia burgdorferi*. *J Appl Ecol* 2013; 50:510–518.
30. Littman MP, Goldstein RE, Labato MA, Lappin MR, Moore GE. ACVIM small animal consensus statement on Lyme disease in dogs: Diagnosis, treatment, and prevention. *J Vet Intern Med* 2006;20: 422–434.
31. Greene C, Straubinger RK, Levy SA. *Infectious Diseases of the Dog and Cat*. 4th ed. St. Louis, Missouri: Elsevier Saunders, 2012.
32. Butler CM, Houwers DJ, Jongejan F, van der Kolk JH. *Borrelia burgdorferi* infections with special reference to horses. A review. *Vet Quart* 2005;27:147–156.
33. Tuomi J, Rantamäki LK, Tanskanen R. Experimental infection of cattle with several *Borrelia burgdorferi sensu lato* strains; immunological heterogeneity of strains as revealed in serological tests. *Vet Microbiol* 1998;60:27–43.
34. Shaw SE, Day MJ, Birtles RJ, Breitschwerdt EB. Tick-borne infectious diseases of dogs. *Trends Parasitol* 2001;17:74–80.
35. Sykes JE. Lyme borreliosis. In: Sykes JE, ed. *Canine and Feline Infectious Diseases*. St. Louis, Missouri: Elsevier Saunders, 2014: 487–497.
36. Peregrine AS, Barker IK, Abrams-Ogg AC, Woods JP. Screening dogs in Ontario for *Borrelia burgdorferi* and *Ehrlichia canis* should be selective rather than routine. *Can Vet J* 2007;48:673.
37. Levy SA, O'Connor TP, Hanscom JL, Shields P, Lorentzen L, Dimarco AA. Quantitative measurement of C6 antibody following antibiotic treatment of *Borrelia burgdorferi* antibody-positive nonclinical dogs. *Clin Vaccine Immunol* 2008;15:115–119.
38. Krupka I, Straubinger RK. Lyme borreliosis in dogs and cats: Background, diagnosis, treatment and prevention of infections with *Borrelia burgdorferi sensu stricto*. *Vet Clin North Am Small Anim Pract* 2010;40:1103–1119.
39. Piesman J. Strategies for reducing the risk of Lyme borreliosis in North America. *Int J Med Microbiol* 2006;296 Suppl 40:17–22.
40. Levy SA, Lissman BA, Ficke CM. Performance of a *Borrelia burgdorferi* bacterin in borreliosis-endemic areas. *J Am Vet Med Assoc* 1993; 202:1834–1838.
41. Klingborg DJ, Hustead DR, Curry-Galvin EA, et al. AVMA Council on biologic and therapeutic agents' report on cat and dog vaccines. *J Am Vet Med Assoc* 2002;221:1401–1407.
42. Mead P, Goel R, Kugeler K. Canine serology as adjunct to human Lyme disease surveillance. *Emerg Infect Dis* 2011;17:1710–1712.